HIV-1 Infection of hematopoietic progenitor cells in vivo in humanized mice.

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Public Summary:
Individuals infected with the AIDS virus (HIV) often show many abnormalities of the blood system, suggesting that infection somehow alters the function of the bone marrow, which is the original source of all blood cell lineages. Currently controversy rages in the field regarding whether HIV directly infects developing blood cells in the bone marrow, or if it manifests these effects indirectly. In this study, we exposed immature developing blood cells, known as hematopoietic progenitor cells, to HIV. In addition, we infected humanized mice, mice engineered to contain a human blood system, with HIV. In both of these cases we noted that HIV infection decreased the ability of bone marrow-derived progenitor cells to form red blood cell and white blood cell colonies, indicating that the presence of HIV perturbed hematopoiesis, the process of forming mature blood cells. In addition we demonstrated direct infection of some early blood cell progenitor cells, indicating that direct infection of these progenitor cells is at least in part responsible for the decrease in bone marrow function seen in HIV disease. These results have important implications regarding reservoirs for virus infection in the body, and for development of stem cell therapeutic strategies for HIV disease.

Scientific Abstract:
HIV infection has been associated with defective hematopoiesis since the earliest days of the HIV/AIDS epidemic. Generation of all hematopoietic lineages suffers in the face of infection. The mechanisms by which HIV impairs normal blood cell development remain unclear and direct infection of intermediate hematopoietic progenitors has not been established as a source of HIV associated hematopoietic pathology. Here, we demonstrate infection of multiple subsets of highly purified intermediate hematopoietic progenitors by wild type HIV both in vitro and in vivo. While direct infection is clearly cytotoxic, we find that some infected progenitors can survive and harbor proviral DNA. We report intermediate hematopoietic progenitors to be a novel target of infection and their permissivity to infection increases with development. Further, the NSG-BLT humanized mouse provides a unique model for studying the impact of HIV infection on bone marrow-based human hematopoiesis.